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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,803	11/24/2006	Shey-Shing Sheu	RO0006US.NP	8858

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LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

NOTIFICATION DATE	DELIVERY MODE
10/09/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/580,803	SHEU ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-54 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-54 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 25 May 2006 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 03/36/07; 11/20/2006.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Abstract of the Disclosure is objected to because is does not meet the requirement of the MPEP for US application. Correction is required. See MPEP 608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Applicant is respectfully requested to amend the abstract because the Abstract is not in US format. .

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

The drawings and particularly the pictures are frequently very small and difficult to understand because of the consequent poor resolution. Larger format Figures, and particularly in those that are pictures, are suggested. In addition Figures 1 and 2 on their face and in their brief descriptions fail to define the experimental conditions for the synthetic process steps labeled with bold face lower case letters; Figures 1 and 2 are therefore incomplete.

The instant disclosure fails to include a complete "Cross-References to Related Applications." See 37 C.F.R. §1.78 and MPEP at §201.11. Applicant is respectfully requested to update the information as the first paragraph of the disclosure to include reference to the parent PCT application.

No claims have been cancelled, no claims have been amended, the disclosure has not been amended at page 1, and no new claims have been added as of the date of this Office action. Two Information Disclosure Statement (2 IDSs) filed March 26, 2007 and November 20, 2006 have been received with all cited non-US Patent references and made of record.

Claims **1-54** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1-54** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims have not met the written description standard of *Regents of the University of California v. Eli Lilly* (119F.3d 1559 at 1568; 43 USPQ2d 1398 at 1406 (Fed. Cir 1997)) which MPEP §2163 at page 2100-162, column 1, quotes as follows: "A definition by function alone 'does not suffice' to describe a coding sequence 'because it is only an indication of what the gene does, rather than what it is.'" Applicant's reliance on generic functional terminology including "amino acid derivative," "peptide comprising," and "having antioxidant activity" wherein the disclosure definition thereof does not overcome the functionality of the noted term or otherwise provide a basis for a complete definition of the metes and bounds of the claimed subject matter in the claim.

Claims **1-54** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for making and testing for an anti-oxidant protective effect of a few choline esters of the compounds glutathione, N-acetyl cysteine, and cysteine, does not reasonably provide enablement for the very large number of alternative structures, the biological testing thereof, and all of the alternative syntheses claimed therefore. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The instant claims are directed to a very large number of compounds the vast majority of which have not been structurally identified, synthesized and/or tested for the capability to inhibit the adverse effects of oxidants on cell functions, with particular emphasis on mitochondrial functions. No claimed compound has been tested to determine activity in the treatment of any specific disease condition.

B. The nature of the invention: This question is dealt with the previous paragraph.

C. The state of the prior art: Compounds are disclosed in the prior art that read on, and therefore anticipate, compounds claimed generically and named specifically in the instant claims. In addition, a combination of references suggest that the claimed method of treatment is obvious in view of the disclosures cited therein.

D. The level of one of ordinary skill: The ordinary practitioner would be expected to know how to make and how to test in a preliminary manner the compounds of the instant claims. But in view of the absence of any disclosure of a test regimen involving a test host (e.g. lower mammals, etc.) accepted in the art as predictive of efficacy against a particular disease condition, there is a low level of skill in determining whether the instant results are extrapolatable to the treatment of actual disease conditions of the kind listed in claim **40** or the effective inhibition of "oxidative stress" the mammalian cell types listed in claims **38 and 45**.

E. The level of predictability in the art: The predictability in the synthetic portion of the instant claims is high in view of the well known methods cited in the instant IDS's. However, the instant disclosure's 11th Example is only prospective, and there are therefore no Examples wherein an actual disease condition has been shown to have been effectively treated by administration of any compound disclosed or claimed herein, thereby rendering the instant method of treatment claims directed to subject matter in an area of medical disease treatment that is highly unpredictable due to the meager amount of relevant test data disclosed herein and of test data disclosed in the prior art.

F. The amount of direction provided by the inventor: The instant disclosure discloses how to make a small number of the compounds disclosed and supplies some biological testing data suggesting that cells treated *in vitro* have a longer life span under oxidative stress than control populations. However, the instant disclosure does not provide any test data permitting one of ordinary skill to believably extrapolate from the test data provided to the plethora of

diseases listed in claim **40**, diseases some of which are well known to be either uncurable including Lou Gehrig's disease ("amyoytophic lateral sclerosis") or at best very difficult to effectively treat including "aging-related diseases" generally.

G. The existence of working examples: This subject is dealt with in the previous paragraph.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because the instant disclosure, while enabling the synthesis of a few compounds and providing a showing that oxidative stress induced in cells in culture (in vitro) can be reduced by administration of a few of the compounds prepared, there is insufficient data to provide a reasonable basis for extrapolation of the biological test data provided to any *in vivo* disease treatments.

The disclosure is objected to because of the following informalities:

At page 6, line 17, the term "recover" is misspelling of the term -- recovery --.

Appropriate correction is required.

Claims **1-10, 13-15, 17-24, 27-28, 30-32, 37-40, 44 and 46-54** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 5, the terms "amino acid" and "amino acid derivative having antioxidant activity" are technically erroneous (R is a substituent, not a separate compound as required by the noted terms) and the noted terms fail to provide any definition of where in the structure of the "R" substituent a bonding attachment occurs to the remainder of the generic formulas (I) and (II), thereby rendering the claim incompletely defined. See also claims **1-10, 13-15, 17-24 and 27-28** wherein the above noted terms plus the terms "linker molecule," "hydrocarbon(s)," "N-heterocycle," "aromatic," and terms including same as their grammatical object. This rejection does not apply when the preceding terms precede the term "group."

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim

does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu,* 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald,* 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall,* 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche,* 86 USPQ 481 (Bd. App. 1949). In the present instance, claim **1** recites the broad recitation "comprising" at line 6, and the claim also recites "compound according to formula (I) or (II)" at line 1 and "containing" at line 8 which are the narrower statements of the ranges/limitations applicable to the substituent definitions.

In claim **13** the term "comprises" renders the claim lacking in proper antecedent basis (compound claims not directed to polymers must be restricted to narrow terms of art because the term "to comprise" means -- to include -- and therefore implies the presence of subject matter not defined in the claim, a variation of this portion of the statute when said term or its grammatical conjugates are present in a compound claim). In addition, claim **13** is improperly dependent because the claim at lines 2-13 is directed to subject matter not provided for in claim **1**. Examiner suggests that the definition of "Z" in claim **1** needs to be expanded in some manner to include the subject matter of claim **13** and the noted term replaced by narrow language in claim **13**.

In claims **30-31** the term "the N-heterocyclic amine comprising a quaternary nitrogen selected from the group consisting of pyridinyl, ... and pirazinyl" and the parallel term in claim **31** are technically erroneous ("pirazinyl" is a misspelling of --pyridazinyl-- or possibly --pyrazinyl --?) and incomplete because the particular structures of the substituents being claimed are not completely described in either claim **30 or 31**; i.e. it is unclear what nitrogen is quaternary or whether multiple quaternary (?) nitrogens are present. Examiner also notes the included term "comprising," a term that renders the instant claims indefinite because said term means "including," a meaning implying that the subsequently list of substituent groups is not a complete description of all of the structural features present. Examiner also noted in conclusion that the term "comprising" renders both noted claims improperly dependent for failure to further limit the scope of the claim from which they depend. Examiner respectfully

requests a more complete structural formula or formulas to provide the minimum guidance necessary to permit the ordinary practitioner to comprehend the chemical structures being claimed.

In claim **32** at line 2, the term "the compound according to claim **1**" is grammatically incorrect. Did applicant intend the term to read -- a compound according to claim **1** --?

In claims **37 and 44** the term "compound is in the form of a pharmaceutical composition" is misleading. Did applicant intend the term to read -- compound is administered as part of a pharmaceutical composition -- or the like?

In claim **40** the terms "neurodegenerative disease," "muscular disorders," "congenital mitochondrial diseases," "neuromuscular degenerative disorders," and "aging-related diseases or disorders" are generic, and because they lack sufficient further definition, these terms render the instant claim incompletely defined.

In claim **46** at lines 6-7, the term "agents that are effective to remove one or more protecting groups" is generic and functional and therefore fails to define either the nature of the chemical groups being removed or the identity/identities of the "agent(s)" being claimed as effective for the purpose, thereby rendering the claimed process incompletely defined. See also claim **47** wherein the terms "one or more protecting groups" and "cation scavenger agent" cause the noted claim to have the same problem.

Note to applicant: The instant process claims appear to be adding steps in the synthetic process in reverse order wherein the term of art "further comprising" is central to the claiming strategy. Examiner suggests that a claim wherein the complete process enabled herein is clearly defined followed by dependent claims directed to individual steps therein is a much less confusing, and therefore more appropriate, approach to claiming this subject matter. Claims **46-54** generally lack clarity due to a confusing claiming strategy and therefore are rejected for this reason under the statute quoted above. Examiner also notes in claims **46, 49, 50 and 51** that the variable " R' " is not well printed and needs to be presented in a larger font size to insure that it is not mistaken for "R."

In claims **51 and 52** examiner finds subject mater apparently related to the subject matter of claims **30-31**. Examiner finds the instant noted claims, like claims **30-31**, to be incomplete

in their description of the process intermediate structures, starting materials, reagents and the structures thereof, and products, limitations that make understanding the subject matter being claimed herein nearly impossible. A clarifying amendment is respectfully requested.

In claim **51** at line 8, the term "I-Q^1" is the only reagent specified, when the structure "VIIIa" clearly suggests that two process steps are required, or that a valence error is present. Clarification is respectfully requested.

In claim **53** the term "protected glutathione" is incomplete because the particular protecting groups have not been identified and the locations thereof have also not been identified, thereby rendering the claim incompletely defined.

In claims **53 and 54** the terms "R' is a protected glutathione" and "R is L-cysteine" are both technically erroneous because both terms are directed to compounds, not substituent groups. In addition, variable "R" in the second term appears to include a typographical error (did applicant intend the term to read -- R' --?; emphasis added to insure clarity).

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **1-54** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-5*** of copending Application No. **11/312,873**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the defined amino acid-choline ester derivatives, the pharmaceutical compositons thereof, the method of treatment wherein said amino acid-choline ester derivatives are admninistered, and the method of making said aminoacids-choline esters, are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **1-54** of this application conflict with claims ***1-5*** of Application No. **11/312,873**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **1-45** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Murphy et al. '532** (PTO-1449 ref. **1A**).

Applicant is referred to claim *1* at column 20, wherein the instant claimed subject matter has been anticipated.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for

unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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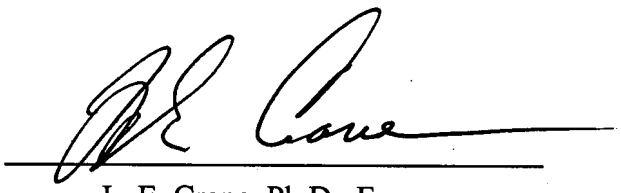
10/01/2007



L. E. Crane, Ph.D., Esq.
Primary Patent Examiner
Technology Center 1600